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EXAMINER

PARVINI, PEGAH

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1793

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/592,017	Applicant(s) KUEBELBECK, ARMIN	
	Examiner PEGAH PARVINI	Art Unit 1793	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 December 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 2 and 4-28 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-2 and 4-28 is/are rejected.
- 7) ☒ Claim(s) 20 and 21 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Any rejection and/or objection made and the previous Office Action and not repeated below, is hereby withdrawn.

Claim Objections

Claims 20 and 21 are objected to because of the following informalities: it appears that Applicants intended to delete “the amine” in the language of said claims since the existence of such do not quite go with the rest of the statements. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 5-19, and 21-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 1036763 to **Teller et al.** in view of U.S. Patent No. 5,932,168 to Su et al.

Regarding claims 1, 5, 7-19 and 22-26, Teller et al. clearly disclose the preparation of monodispersed polysilicic acid particles (i.e. silica particles) by simultaneous or step-wise dosage of precursor materials such as tetraalkoxysilane and

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terminal silane fluorescent dye in hydrolysis medium of alcohol, ammonium and water (Abstract, [0001]-[0007]); the reference is drawn to polycondensation between the precursor tetraalkoxysilane and terminal silylated (fluorescence) coloring material ([0013]). Teller et al. disclose that the silica particles obtained have a size of from 0.05 μ m to 10 μ m ([0006]). The reference, also, discloses that the medium comprises water, alcohol (i.e. the solubilizer) and ammonia (i.e. base) ([0007] and Examples). Moreover, Teller et al. teach the use of tetraethoxysilane or TEOS as the tetraalkoxysilane used (Examples). Additionally, the reference discloses conducting the polycondensation hydrolysis in a temperature range of 40°C to 70°C ([0013]). It is noted that there is overlapping ranges of temperature with the ones instant claimed; overlapping ranges have been held to establish *prima facie* obviousness. See MPEP § 214405.

Furthermore, Teller et al. disclose a substantially identical structure for the terminally silylated (fluorescent) dye as that recited in claims 12-16 ([0007]-[0012]). In addition, Teller et al. disclose that such particles are used in different modifications in the molecular biology, purification of nucleic acid and proteins, as solid phase for the investigation of molecular recognition phenomena ([0002]).

With reference to the production of “non-porous particles”, it is noted that since the Teller et al. do not disclose the production of porous particles, therefore, it is seen to read on the instant limitation (i.e. non-porous silica).

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Teller et al. although disclosing the use of base in the polycondensation hydrolysis process of making silica particles, do not expressly disclose the use of a base such as ethylenediamine or aminoethanol.

However, Su et al. disclose the use of bases such as N-(2-hydroxyethyl) ethylenediamine or a combination of a number of bases along with water for hydrolyzing of alkoxy silane compound (e.g. tetraalkoxysilane) to produce silica (column 5, lines 40-67). Therefore, it would have been obvious to one of ordinary skill in the art to modify Teller et al. in order to include the use of a base such as N-(2-hydroxyethyl) ethylenediamine, ammonium hydroxide, etc. in the medium used for hydrolyzing tetraalkoxysilane as that taught by Su et al. motivated by the fact that not only Su et al. and Teller et al. are from relevant field of art, but also, the ammonia and N-(2-hydroxyethyl) ethylenediamine, as shown in Teller et al. and Su et al., respectively, have been both utilized in hydrolysis processes specifically drawn to the production of silica particles. Therefore, they can be seen as functionally equivalent since they are both bases used in similar processes. It is noted that the substitution of the functionally equivalent compound is well within the scope of the skilled artisan absent clear and specific evidence proving why N-(2-hydroxyethyl) ethylenediamine (i.e. base) of Su et al. can not, under any circumstances, be substituted for the ammonia (i.e. base) of Teller et al. absent clear and specific evidence showing the contrary.

Regarding claims 6, 21 and 27-28, Teller et al. in Example 1, disclose the use of 76.6 ml ethanol, 13.6 ml 25% ammonia, 20 ml water, and 11.2 ml TEOS; utilizing the

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density values of components, the content of said components in weight, and consequently, the weight percentages of said components were calculated and found to be 64% ethanol, 2.4% ammonia, 21% water, and 11% TEOS. It is noted that there is overlapping ranges with the percentages instantly claimed.

Again, it would have been obvious to substitute N-(2-hydroxyethyl) ethylenediamine of Su et al. for ammonia as detailed out above; therefore, it is the examiner's position that the proportion of N-(2-hydroxyethyl) ethylenediamine would be close to the proportion of ammonia motivated by the fact that the substitution of the functionally equivalent compounds for the same purpose is well within the scope of the skilled artisan absent clear and specific evidence proving that N-(2-hydroxyethyl) ethylenediamine (i.e. base) of Su et al. can not, under any circumstances, be substituted for the ammonia (i.e. base) of Teller et al. considering the fact that Su et al. is reasonably pertinent to the particular problem with which the applicants were concerned.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Teller et al. in view of Su et al. as applied to claim 1 above, and in further view of U.S. Patent No. 6,302,926 to Anselmann et al.

The combination of Teller et al. in view of Su et al. discloses the preparation of monodispersed polysilicic acid particles (i.e. silica particles) by simultaneous or step-wise dosage of precursor materials such as tetraalkoxysilane and terminal silane fluorescent dye in hydrolysis medium of alcohol, ammonium and water wherein the

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ammonium base may be replaced by another base such as N-(2-hydroxyethyl) ethylenediamine as detailed out above.

However, with reference to bringing the particle size to the desired size by continuous metered addition of corresponding silane (i.e. tetraalkoxysilane), it is noted that Teller et al. disclose simultaneous or step-wise dosage of precursor materials such as tetraalkoxysilane and terminal silane fluorescent dye in the medium. Although Teller et al. may not expressly disclose that metering the addition of tetraalkoxysilane into the medium would control the particle size to bring it to the desired particle size, this is found obvious to control the particle size by such method as that evidenced by Anselmann et al. (column 3, lines 1-10) motivated by the fact that Anselmann et al. is drawn to the same field of art as evidenced all throughout the reference. Anselmann et al. disclose the production of monodispersed silica particles by hydrolysis polycondensation of tetraalkoxysilane. Therefore, it would have been obvious to modify Teller et al. in view of Su et al. to disclose the metering addition of tetraalkoxysilane motivated by the fact that Anselmann et al. clearly disclose that metering the addition of tetraalkoxysilane into the medium would control the particle size to bring it to the desired particle size; furthermore, motivated by the fact that Teller et al. disclose simultaneous or step-wise dosage of precursor materials such as tetraalkoxysilane and terminal silane fluorescent dye in the medium.

Claims 1, 4, 6-19, 20-21, and 22-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 1036763 to **Teller et al.** in view of U.S. Patent No. 5,626,964 to Blizzard et al.

Regarding claims 1, 4, 7-19 and 22-26, Teller et al. clearly disclose the preparation of monodispersed polysilicic acid particles (i.e. silica particles) by simultaneous or step-wise dosage of precursor materials such as tetraalkoxysilane and terminal silane fluorescent dye in hydrolysis medium of alcohol, ammonium and water (Abstract, [0001]-[0007]); the reference is drawn to polycondensation between the precursor tetraalkoxysilane and terminal silylated (fluorescence) coloring material ([0013]). Teller et al. disclose that the silica particles obtained have a size of from 0.05 μ m to 10 μ m ([0006]). The reference, also, discloses that the medium comprises water, alcohol (i.e. the solubilizer) and ammonia (i.e. base) ([0007] and Examples). Moreover, Teller et al. teach the use of tetraethoxysilane or TEOS as the tetraalkoxysilane used (Examples). Additionally, the reference discloses conducting the polycondensation hydrolysis in a temperature range of 40°C to 70°C ([0013]). It is noted that there is overlapping ranges of temperature with the ones instant claimed; overlapping ranges have been held to establish *prima facie* obviousness. See MPEP § 2144.05.

Furthermore, Teller et al. disclose a substantially identical structure for the terminally silylated (fluorescent) dye as that recited in claims 12-16 ([0007]-[0012]). In addition, Teller et al. disclose that such particles are used in different modifications in

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the molecular biology, purification of nucleic acid and proteins, as solid phase for the investigation of molecular recognition phenomena ([0002]).

With reference to the production of “non-porous particles”, it is noted that since the reference does not disclose the production of porous particles; therefore, it is seen to read on the instant limitation.

Teller et al. although disclosing the use of base in the polycondensation hydrolysis process of making silica particles, do not expressly disclose the use of a base such as ethylenediamine or aminoethanol.

However, Blizzard et al. disclose the hydrolysis and condensation of tetraethoxysilane which is initiated by water in the presence of ethanolamine (column 7, line 60 to column 8, line 14) and pentaerythritol tetra-acrylate which is a ketone (i.e. solubilizer). Therefore, it would have been obvious to one of ordinary skill in the art to modify Teller et al. in order to include the use of a base such as ethanolamine in the medium used for the process of hydrolysis and condensation of tetraalkoxysilane as that taught by Blizzard et al. motivated by the ammonia and ethanolamine, as shown in Teller et al. and Blizzard et al. have been both utilized in hydrolysis and condensation processes of tetraalkoxy silane in the presence of water; therefore, they can be seen as functionally equivalent. It is noted that the substitution of the functionally equivalent compounds is well within the scope of the skilled artisan absent clear and specific evidence showing why ethanolamine (i.e. base) of Blizzard et al. can not, under any circumstances, be substituted for the ammonia (i.e. base) of Teller et al. It is, additionally, noted that the example of Blizzard et al. is pertinent to the art of Teller et al.

Regarding claims 6, 21 and 27-28, Teller et al. in Example 1, disclose the use of 76.6 ml ethanol, 13.6 ml 25% ammonia, 20 ml water and 11.2 ml TEOS; using the density of said components, the content of said components in weight, and consequently, the weight percentages of said components were calculated and found to be 64% ethanol, 2.4% ammonia, 21% water, and 11% TEOS. It is noted that there is overlapping ranges of said values with the ones instantly claimed.

Again, it would have been obvious to substitute ethanolamine for ammonia in Teller et al. since the substitution of the functionally equivalent compounds is well within the scope of the skilled artisan absence clear and specific evidence showing why ethanolamine (i.e. base) of Blizzard et al. can not, under any circumstances, be substituted for the ammonia (i.e. base) of Teller et al. considering the fact that Blizzard et al. is reasonably pertinent to the particular problem with which the applicants were concerned.

Regarding claim 20, Blizzard et al. in Example 1 (columns 7-8) disclose 10.24g TEOS, 0.775 g ethanolamine, 73.7 g pentaerythritol tetra-acrylate which is a ketone (i.e. solubilizer) and 4.36 g water; thus, the weight percentages of each the components is found to be about 11% TEOS, 0.87% ethanolamine, 82% pentaerythritol tetra-acrylate, and 4.89% water. There are overlapping ranges of said components with the ones instantly claimed; overlapping ranges have been held to establish *prima facie* obviousness. See MPEP § 2144.05.

As shown above, Blizzard et al. is reasonably pertinent to the particular problem with which the applicants were concerned, and it is obvious to substitute ethanolamine for ammonia since the substitution of the functionally equivalent compounds is well within the scope of the skilled artisan absent clear and specific evidence showing why ethanolamine of Blizzard et al. can not, under any circumstances, be substituted for the ammonia (i.e. base) of Teller et al. considering the fact that Blizzard et al. is reasonably pertinent to the particular problem with which the applicants were concerned.

In fact, Blizzard et al. utilize the same group of compounds to conduct the hydrolysis of TEOS in a medium. Therefore, the combination of Teller et al. in view of Blizzard et al. is seen to read on the limitation of instant claims 6, 20-21 and 27-28 as detailed out in the above paragraph as well.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Teller et al. in view of Blizzard et al. as applied to claim 1 above, and in further view of U.S. Patent No. 6,302,926 to Anselmann et al.

The combination of Teller et al. in view of Blizzard et al. discloses the preparation of monodispersed polysilicic acid particles (i.e. silica particles) by simultaneous or step-wise dosage of precursor materials such as tetraalkoxysilane and terminal silane fluorescent dye in hydrolysis medium of alcohol, ammonium and water wherein the ammonium base may be replaced by another base such as aminoethanol as detailed out above.

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However, with reference to bringing the particle size to the desired size by continuous metered addition of corresponding silane (i.e. tetraalkoxysilane), it is noted that Teller et al. disclose simultaneous or step-wise dosage of precursor materials such as tetraalkoxysilane and terminal silane fluorescent dye in the medium. Although said reference may not expressly disclose that metering the addition of corresponding silane in order to control the particle size of silica, this is found obvious to control the particle size of silica using metering the addition of tetraalkoxysilane or corresponding silane as that evidenced by Anselmann et al. (column 3, lines 1-10). It is noted that Anselmann et al. is drawn to the same field of art as evidenced all throughout the reference and disclose the production of monodispersed silica particles by hydrolysis polycondensation of tetraalkoxysilane. Therefore, it would have been obvious to modify Teller et al. in combination with Blizzard et al. in order to include the particle size control of silica through metering the addition of tetraalkoxysilane motivated by the fact that Anselmann et al. clearly discloses that metering the addition of tetraalkoxysilane into the medium would control the particle size of silica to bring it to the desired particle size; furthermore, motivated by the fact that Teller et al. disclose simultaneous or step-wise dosage of precursor materials such as tetraalkoxysilane and terminal silane fluorescent dye in the medium.

Claims 1, 5, 7-8, 10-18 and 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent Application Publication No. 2003/0124564 to **Trau et al.** in view of Su et al.

Regarding claims 1, 5, 7-8, 10-18, and 24-26, Trau et al. disclose the Stöber process through which monodispersed silica particles are formed in a hydrolysis of tetraethyl orthosilicate (TEOS) in a solution of ethanol, water, and ammonia having a maximum particle size of approximately 3 microns ([0010]-[0012]). Moreover, the reference discloses that Stöber process allows the incorporation of fluorescent dyes into the silica network ([0012]; Figure 3). As can be seen, the structure of Figure 3 clearly teaches the limitation of instant claims 10-16; for example, R¹, R², and R³ are identical and are methoxy groups (i.e. alkoxy groups), and part of the structure containing one carbon bonded to two nitrogens through single bonds and bonded to sulfur through a double-bond is B (i.e. aminothiocarbonyl group). Furthermore, A¹ is the two carbon chain connecting the silicon to nitrogen of B. In addition, the part of the structure of which corresponds to the three rings corresponds to A² which would impart color (i.e. dye) upon exposure to light. Finally, the segment of one benzene ring bonded to a carboxylic group is C.

With reference to the production of “non-porous particles”, it is noted that since the reference does not disclose the production of porous particles, therefore, it is seen to read on the instant limitation (i.e. non-porous silica).

Trau et al. although disclosing the use of base in the Stöber process, do not expressly disclose that said base may be ethylenediamine or aminoethanol.

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However, Su et al. disclose the use of bases such as N-(2-hydroxyethyl) ethylenediamine or a combination of a number of bases along with water in a medium used for hydrolyzing of alkoxy silane compound (e.g. tetraalkoxysilane) to produce silica particles (column 5, lines 40-67). Therefore, it would have been obvious to one of ordinary skill in the art to modify Trau et al. in order to include the use of a base such as N-(2-hydroxyethyl) ethylenediamine, ammonium hydroxide, etc. in the medium used for hydrolyzing tetraalkoxysilane as that taught by Su et al. motivated by the fact that not only Su et al. and Trau et al. (in particular the Stöber process) are from relevant field of art, but also, the ammonia and N-(2-hydroxyethyl) ethylenediamine, as shown in Teller et al. and Su et al. respectively, have been both utilized in hydrolysis processes specifically drawn to the production of silica particles. Thus, said bases can be seen as functionally equivalent. It is noted that the substitution of the functionally equivalent compounds is well within the scope of the skilled artisan absent clear and specific evidence showing why N-(2-hydroxyethyl) ethylenediamine (i.e. base) of Su et al. can not, under any circumstances, be substituted for the ammonia (i.e. base) of Stöber process of Trau et al.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Trau et al. in view of Su et al., as applied to claim 1 above, and in further view of U.S. Patent No. 6,302,926 to Anselmann et al.

The combination of Trau et al. in view of Su et al. disclose the production of monodispersed silica particles using Stöber process through which monodispersed

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silica particles are formed in a hydrolysis of tetraethyl orthosilicate (TEOS) in a solution of ethanol, water, and ammonia having a maximum particle size of approximately 3 microns wherein the ammonia base may be replaced by another base such as N-(2-hydroxyethyl) ethylenediamine as detailed out above.

With reference to bringing the particle size to the desired size by continuous metered addition of corresponding silane (i.e. tetraalkoxysilane), although the references may not expressly disclose controlling the particle size of silica by metering addition of the corresponding silane such as tetraalkoxysilane, this is found obvious to control the particle size of silica by metering addition of the corresponding silane as that evidenced by Anselmann et al. (column 3, lines 1-10). It is noted that Anselmann et al. is drawn to the same field of art as evidenced all throughout the reference and disclosed the production of monodispersed silica particles by hydrolysis polycondensation of tetraalkoxysilane. Therefore, it would have been obvious to modify Trau et al. in combination with Su et al. to expressly disclose the metering addition of tetraalkoxysilane motivated by the fact that Anselmann et al. clearly disclose that metering the addition of tetraalkoxysilane into the medium would control the particle size of silica to bring it to the desired particle size.

Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Trau et al. in view of Su et al., as applied to claim 1 above, and in further view of Teller et al.

The combination of Trau et al. and Su et al. disclose the production of monodispersed silica particles using Stöber process through which monodispersed

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silica particles are formed in a hydrolysis of tetraethyl orthosilicate (TEOS) in a solution of ethanol, water, and ammonia having a maximum particle size of approximately 3 microns as detailed above wherein ammonia may be replaced by other amine bases such as N-(2-hydroxyethyl) ethylenediamine as detailed out above.

However, said references do not expressly disclose that the produced silica particles may be utilized in any of the areas disclosed in instant claim 19.

Nevertheless, it would have been obvious to modify Trau et al. to disclose the use of said monodispersed silica particles of smaller than 3 microns produced by Stöber process in an area recited in claim 19 such as a solid phase for the investigation of molecular recognition phenomena as that taught by Teller et al. motivated by the fact that Teller et al. disclose that such particles are used in different modifications in the molecular biology, purification of nucleic acid and proteins, as solid phase for the investigation of molecular recognition phenomena (Teller et al. [0002]), and further, motivated by the fact that the references are from the same field of endeavor, and particularly, Teller et al. is drawn to the production of silica particles via hydrolysis polycondensation. Thus, it would have been obvious to utilize the silica particles of Trau et al. in view of Su et al. in the area disclosed by Teller et al. since the particles of the two references are produced by substantially similar process and are of substantially overlapping particle size.

Claims 1, 4, 6-8, 10-18, 20-21 and 24-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent Application Publication No. 2003/0124564 to **Trau et al.** in view of Blizzard et al.

Regarding claims 1, 4, 7-8, 10-18, and 24-26, Trau et al. disclose the Stöber process through which monodispersed silica particles are formed in a hydrolysis of tetraethyl orthosilicate (TEOS) in a solution of ethanol, water, and ammonia having a maximum particle size of approximately 3 microns ([0010]-[0012]). Moreover, the reference discloses that Stöber process allows the incorporation of fluorescent dyes into the silica network ([0012]; Figure 3). As can be seen, the structure of Figure 3 clearly teaches the limitation of instant claims 10-16; for example, R¹, R², and R³ are identical and are methoxy groups (i.e. alkoxy groups), and part of the structure containing carbon single bonded to two nitrogens and double bonded to sulfur is B (i.e. aminothiocarbonyl group). Furthermore, A¹ is the two carbon chain connecting the Si to N of the aminothiocarbonyl group. In addition, the part of the structure which corresponds to the three rings corresponds to A² which would impart color (i.e. dye) upon exposure to light. Finally, the segment of one benzene ring bonded to a carboxylic group is C.

With reference to the production of “non-porous particles”, it is noted that since the reference does not disclose the production of porous particles, therefore, it is seen to read on the instant limitation (i.e. non-porous silica).

Trau et al. although disclosing the use of base in the Stöber process, do not expressly disclose that said base may be ethylenediamine or aminoethanol.

However, Blizzard et al. disclose the hydrolysis and condensation of tetraethoxysilane which is initiated by water in the presence of ethanolamine (column 7, line 60 to column 8, line 14). Therefore, it would have been obvious to one of ordinary skill in the art to modify Trau et al. in order to include the use of a base such as ethanolamine in the medium used for the process of hydrolysis and condensation of tetraalkoxysilane as that taught by Blizzard et al. motivated by the ammonia and ethanolamine, as shown in Trau et al. and Blizzard et al. respectively, have been both utilized in hydrolysis and condensation processes of tetraalkoxy silane in the presence of water; therefore, they can be seen as functionally equivalent. It is noted that the substitution of the functionally equivalent compounds is well within the scope of the skilled artisan absent clear and specific evidence showing why ethanolamine (i.e. base) of Blizzard et al. can not, under any circumstances, be substituted for the ammonia (i.e. base) of Trau et al. absent clear and specific evidence showing the contrary. It is, additionally, noted that the example of Blizzard et al. is clearly pertinent to the art of Trau et al.

Regarding claims 6, 20-21 and 27-28, Blizzard et al. in Example 1 (columns 7-8) disclose 10.24g TEOS, 0.775 g ethanolamine, 73.7 g pentaerythritol tetra-acrylate which is a ketone (i.e. solubilizer), and 4.36 g water; thus, the weight percentages of each the components is found to be about 11% TEOS, 0.87% ethanolamine, 82% pentaerythritol tetra-acrylate, and 4.89% water. There are overlapping ranges of said

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components with the ones instantly claimed; overlapping ranges have been held to establish *prima facie* obviousness. See MPEP § 2144.05.

As shown above, Blizzard et al. is from the same field of endeavor and it is obvious to substitute ethanolamine for ammonia since the substitution of the functionally equivalent compounds is well within the scope of the skilled artisan. Absence of clear and specific evidence showing why ethanolamine of Blizzard et al. can not, under any circumstances, be substituted for the ammonia (i.e. base) of Trau et al. considering the fact that Blizzard et al. is reasonably pertinent to the particular problem with which the applicants were concerned.

In fact, Blizzard et al. utilize the same group of compounds to conduct the hydrolysis of TEOS in a similar medium. Therefore, the combination of Trau et al. in view of Blizzard et al. is seen to read on the limitation of instant claims 6, 20-21 and 27-28 as detailed out in the above paragraph as well.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Trau et al. in view of Blizzard et al., as applied to claim 1 above, and in further view of U.S. Patent No. 6,302,926 to Anselmann et al.

The combination of Trau et al. in view of Blizzard et al. disclose the production of monodispersed silica particles using Stöber process through which monodispersed silica particles are formed in a hydrolysis of tetraethyl orthosilicate (TEOS) in a solution of ethanol, water, and ammonia having a maximum particle size of approximately 3

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microns wherein the ammonia base may be replaced by another base such as aminoethanol as detailed out above.

With reference to bringing the particle size of silica to a desired size by continuously metering the addition of corresponding silane (i.e. tetraalkoxysilane), although the references may not expressly disclose the continuously metering the addition of corresponding silane to control the particle size to bring it to the desired particle size, this is found obvious to control the particle size by doing so since it is evidenced by Anselmann et al. (column 3, lines 1-10) which is drawn to the same field of art as can be seen all throughout the reference. In other words, Anselmann et al. disclose the production of monodispersed silica particles by hydrolysis polycondensation of tetraalkoxysilane. Therefore, it would have been obvious to modify Trau et al. in combination with Blizzard et al. in order to disclose the metering addition of tetraalkoxysilane into the medium to control the particle size of silica motivated by the fact that Anselmann et al. clearly disclose that metering addition of tetraalkoxysilane into the medium would control the particle size so to bring it to a desired particle size.

Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Trau et al. in view of Blizzard et al. as applied to claim 1 above, and in further view of Teller et al.

The combination of Trau et al. and Blizzard et al. discloses the production of monodispersed silica particles using Stöber process through which monodispersed silica particles are formed via hydrolysis of tetraethyl orthosilicate (TEOS) in a solution

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of ethanol, water, and ammonia wherein the silica particles have a maximum particle size of approximately 3 microns, and wherein ammonia may be replaced by other amine bases such as aminoethanol (i.e. ethanolamine) as detailed out above.

However, said references do not expressly disclose that the produced silica particles may be utilized in any of the areas disclosed in instant claim 19.

Nevertheless, it would have been obvious to modify Trau et al. in view of Blizzard et al. to disclose the use of said monodispersed silica particles of smaller than 3 microns produced by Stöber process in an area of claim 19 such as a solid phase for the investigation of molecular recognition phenomena as that taught by Teller et al. motivated by the fact that Teller et al. disclose that such particles are used in different modifications in the molecular biology, purification of nucleic acid and proteins, as solid phase for the investigation of molecular recognition phenomena (Teller et al. [0002]), and further, motivated by the fact that Trau et al. and Teller et al. are from the same field of endeavor. Thus, it would have been obvious to utilize the silica particles of Trau et al. in view of Blizzard et al. in the area disclosed by Teller et al. since the particles of the two references are produced by substantially similar process and are of substantially overlapping particle size.

Claims 1-2, 5, 7-9, 17-19, and 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 4,775,520 to **Unger et al.** in view of Su et al.

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Regarding Claims 1-2, 5, 7-9, 17-19, and 22-23, Unger et al. teach a process through which monodispersed non-porous spherical SiO₂ particles are prepared by, first a sol or primary particles which is prepared by hydrolytic polycondensation of tetraalkoxysilanes in an aqueous/alcoholic ammoniacal medium. Then, the SiO₂ particles are converted to the desired particle size by a continuous measured addition of tetraalkoxysilane or organotrialkoxysilane controlled by the extent of the reaction (Abstract; column 3, lines 5-16; column 4, lines 3-7 and 29-40). Unger et al. disclose the use of alcohol (i.e. solubilizer) such as methanol, ethanol and others, water and ammonia in the process (column 3, lines 46-51; column 4, lines 3-6). Unger et al. teach that suitable tetraalkoxysilanes are esters of aliphatic alcohols containing 1-5 C atoms such as, for example, methanol, ethanol, n- or i-propanol; additionally, Unger et al. discloses that the especially preferred one is tetraethoxysilane (column 3, lines 30-44). Unger et al. teach maintaining the temperature of the process between about 35°C to 75°C (column 4, lines 19-20). Unger et al. disclose obtaining SiO₂ particles with mean particle diameter of 0.05 and 10 microns (column 2, lines 41-43).

In addition, Unger et al. teach that the use of said silica in sorption materials in chromatography of biological molecules of high molecular weight such as, for instance, proteins and nucleic acids (column 3, lines 20-27).

Unger et al. although disclosing the use of base in said process of making silica particles, do not expressly disclose the use of a base such as ethylenediamine or aminoethanol.

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However, Su et al. disclose the use of bases such as N-(2-hydroxyethyl) ethylenediamine or a combination of a number of bases along with water for hydrolyzing of alkoxy silane compound (e.g. tetraalkoxysilane) to produce silica (column 5, lines 40-67). Therefore, it would have been obvious to one of ordinary skill in the art to modify Unger et al. in order to include the use of a base such as N-(2-hydroxyethyl) ethylenediamine, ammonium hydroxide, etc. in the medium used for hydrolyzing tetraalkoxysilane as that taught by Su et al. motivated by the fact that not only Su et al. and Unger et al. are from relevant field of art, but also, the ammonia and N-(2-hydroxyethyl) ethylenediamine, as shown in Unger et al. and Su et al. respectively, have been both utilized in hydrolysis processes specifically drawn to the production of silica particles. Therefore, they can be seen as functionally equivalent. It is noted that the substitution of the functionally equivalent compounds is well within the scope of the skilled artisan absent clear and specific evidence showing why N-(2-hydroxyethyl) ethylenediamine (i.e. base) of Su et al. can not, under any circumstances, be substituted for the ammonia (i.e. base) of Unger et al.

Claims 10-16 and 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Unger et al. in view of Su et al. as applied to claim 1 above, and further in view of Trau et al.

Regarding claims 10-16 and 24-26, the combination of Unger et al. in view of Su et al. as detailed above, disclose a method for the preparation of non-porous spherical

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SiO₂ particles by hydrolytic polycondensation of tetraalkoxysilanes in an aqueous/alcoholic ammoniacal medium, in which method a sol of primary particles is first produced and the SiO₂ particles obtained are then converted to the desired size by a continuous measured addition of tetraalkoxysilane controlled by the extent of the reaction wherein the amine base compound utilized in said process may be N-(2-hydroxyethyl) ethylenediamine as detailed above.

Even though Unger et al. teach that the use of said silica in sorption materials in chromatography of biological molecules of high molecular weight such as, for instance, proteins and nucleic acids, Unger et al. in view of Su et al. do not disclose the specific limitations of claims 12-16 with reference to a fluorescent dye and its structure.

Trau et al. disclose the Stöber process through which monodispersed silica particles are formed in a hydrolysis of tetraethyl orthosilicate (TEOS) in a solution of ethanol, water, and ammonia having a maximum particle size of approximately 3 microns ([0010]-[0012]). Moreover, the reference discloses that Stöber process allows the incorporation of fluorescent dyes into the silica network ([0012]; Figure 3). As can be seen, the structure of Figure 3 clearly teaches the limitation of instant claims 10-16; for example, R¹, R², and R³ are identical and are methoxy groups (i.e. alkoxy groups), and part of the structure containing one carbon bonded to two nitrogens through single bonds and bonded to sulfur through a double-bond is B (i.e. aminothiocarbonyl group). Furthermore, A¹ is the two carbon chain connecting the silicon to nitrogen of B. In addition, the part of the structure of which corresponds to the three rings corresponds to

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A² which would impart color (i.e. dye) upon exposure to light. Finally, the segment of one benzene ring bonded to a carboxylic group is C.

Therefore, at the time of the invention, it would have been obvious to one of ordinary skill in the art to modify Unger et al. in order to include the incorporation of a fluorescent dye as that taught by Stöber process in Trau et al. motivated by the fact that Stöber process is on the preparation of monodispersed silica particles produced by a very similar method as disclosed by Unger et al. in view of Su et al. which would result in particles having overlapping ranges with the ones disclosed by Unger et al.

Claims 1-2, 5, 7-9, 17-19, and 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 4,775,520 to **Unger et al.** in view of Blizzard et al.

Regarding Claims 1-2, 5, 7-9, 17-19, and 22-23, Unger et al. teach a process through which monodispersed non-porous spherical SiO₂ particles are prepared by, first a sol or primary particles which is prepared by hydrolytic polycondensation of tetraalkoxysilanes in an aqueous/alcoholic ammoniacal medium. Then, the SiO₂ particles are converted to the desired particle size by a continuous measured addition of tetraalkoxysilane or organotrialkoxysilane controlled by the extent of the reaction (Abstract; column 3, lines 5-16; column 4, lines 3-7 and 29-40). Unger et al. disclose the use of alcohol (i.e. solubilizer) such as methanol, ethanol and others, water and ammonia in the process (column 3, lines 46-51; column 4, lines 3-6). Unger et al. teach that suitable tetraalkoxysilanes are esters of aliphatic alcohols containing 1-5 C atoms

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such as, for example, methanol, ethanol, n- or i-propanol; additionally, Unger et al. discloses that the especially preferred one is tetraethoxysilane (column 3, lines 30-44). Unger et al. teach maintaining the temperature of the process between about 35°C to 75°C (column 4, lines 19-20). Unger et al. disclose obtaining SiO₂ particles with mean particle diameter of 0.05 and 10 microns (column 2, lines 41-43).

In addition, Unger et al. teach that the use of said silica in sorption materials in chromatography of biological molecules of high molecular weight such as, for instance, proteins and nucleic acids (column 3, lines 20-27).

Unger et al. although disclosing the use of base in said process of making silica particles, do not expressly disclose the use of a base such as ethylenediamine or aminoethanol.

However, Blizzard et al. disclose the hydrolysis and condensation of tetraethoxysilane which is initiated by water in the presence of ethanolamine and pentaerythriol tetra-acrylate which is a ketone (i.e. solubilizer) (column 7, line 60 to column 8, line 14). Therefore, it would have been obvious to one of ordinary skill in the art to modify Unger et al. in order to include the use of a base such as ethanolamine in the medium used for the process of hydrolysis and condensation of tetraalkoxysilane as that taught by Blizzard et al. motivated by fact that ammonia and ethanolamine, as shown in Unger et al. and Blizzard et al. respectively, have been both utilized in hydrolysis and condensation processes of tetraalkoxy silane in the presence of water; therefore, they can be seen as functionally equivalent. It is noted that the substitution of the functionally equivalent compounds is well within the scope of the skilled artisan

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absence clear and specific evidence showing why ethanolamine (i.e. base) of Blizzard et al. can not, under any circumstances, be substituted for the ammonia (i.e. base) of Unger et al. It is, additionally, noted that both references are drawn to pertinent filed of art, hydrolysis condensation of tetraalkoxysilane.

Claims 10-16 and 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Unger et al. in view of Blizzard et al. as applied to claim 1 above, and further in view of Trau et al.

Regarding claims 10-16 and 24-26, the combination of Unger et al. in view of Blizzard et al. as detailed above, disclose a method for the preparation of non-porous spherical SiO₂ particles by hydrolytic polycondensation of tetraalkoxysilanes in an aqueous/alcoholic ammoniacal medium, in which method a sol of primary particles is first produced and the SiO₂ particles obtained are then converted to the desired size by a continuous measured addition of tetraalkoxysilane controlled by the extent of the reaction wherein the amine base compound utilized in said process may be aminoethanol as detailed out above.

Even though Unger et al. teach that the use of said silica in sorption materials in chromatography of biological molecules of high molecular weight such as, for instance, proteins and nucleic acids, Unger et al. in view of Blizzard et al. do not disclose the specific limitations of claims 12-16 with reference to a fluorescent dye and its structure.

Trau et al. disclose the Stöber process through which monodispersed silica particles are formed in a hydrolysis of tetraethyl orthosilicate (TEOS) in a solution of ethanol, water, and ammonia having a maximum particle size of approximately 3 microns ([0010]-[0012]). Moreover, the reference discloses that Stober process allows the incorporation of fluorescent dyes into the silica network ([0012]; Figure 3). As can be seen, the structure of Figure 3 clearly teaches the limitation of instant claims 10-16; for example, R¹, R², and R³ are identical and are methoxy groups (i.e. alkoxy groups), and part of the structure containing one carbon bonded to two nitrogens through single bonds and bonded to sulfur through a double-bond is B (i.e. aminothiocarbonyl group). Furthermore, A¹ is the two carbon chain connecting the silicon to nitrogen of B. In addition, the part of the structure of which corresponds to the three rings corresponds to A² which would impart color (i.e. dye) upon exposure to light. Finally, the segment of one benzene ring bonded to a carboxylic group is C.

Therefore, at the time of the invention, it would have been obvious to one of ordinary skill in the art to modify Unger et al. in view of Blizzard et al. in order to include the incorporation of a fluorescent dye as that taught by Stöber process in Trau et al. motivated by the fact that Stöber process is on the preparation of monodispersed silica particles produced by the same method as disclosed by Unger et al. which would result in particles having overlapping ranges with the ones disclosed by Unger et al.

Response to Amendment

Applicants' amendment to claims 1-2 and 4-19, filed December 22, 2008, is acknowledged. However said amendments do not place the application in condition for allowance as set forth above and addressed in the Response to Arguments below.

Applicants' amendment to claims 1-16 and 18, filed December 22, 2008, by changing the British spelling of certain terminologies to American English spelling or by cancelling the terms which included British spelling is acknowledged. As such, the objection made to such claims as generally set forth in the previous Office action is hereby withdrawn.

Applicants' amendment to claim 17, filed December 22, 2008, by correcting the language of said claim is acknowledged. As such, the objection made to said claim is hereby withdrawn.

Applicants' amendment to claims 6, 12-16 and 19, filed December 22, 2008 is acknowledged. As such, the rejection of said claims under 112-second paragraph and the rejection of claim 19 under 35 U.S.C. 101 are hereby withdrawn.

Response to Arguments

Applicants' arguments filed December 22, 2008 have been fully considered but they are not persuasive.

Since a number of arguments are drawn to claims as amended, they are not deemed to be responded.

In response to applicants' arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections

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are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants have argued that Trau et al. do not disclose the features of claim 14. The examiner disagrees and, respectfully, submits that pages 10-11 of the previous Office action clearly points to Figure 3 which fully encompass claim 14 limitation as also described in details above. It is further noted that the Office action states that "n may be zero as defined in claim 12". Furthermore, although the Office action may not expressly gone through the details of Figure 3 to indicate the structure corresponding to "C" as recited in claim 14, the Office action clearly discloses Figure 3, and R¹, R², R³, A¹, A², C and B are apparent from Figure 3.

In response to applicants' argument that Su et al. is nonanalogous art, it has been held that a prior art reference must either be in the field of applicants' endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicants were concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, Su et al. disclose providing silica by mixing tetraalkoxysilane, water, and ammonium hydroxide (i.e. base) in which water and the base hydrolyze the alkoxy silane, and in fact, the base is used as a catalyzer; furthermore, the reference discloses N-(2-hydroxyethyl) ethylenediamine as one of the suitable bases used for this purpose (column 5, lines 40-67). It is well established that silica sol is a mullite precursor; thus, the mere fact that Su et al. disclose the production of silica in relation to be used in

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mullite is not seen to make Su et al. nonanalogous art. As shown in the segment indicated above, Su et al. is seen to also relate to the production of silica. Thus, the production of silica and the use of certain bases such as N-(2-hydroxyethyl) ethylenediamine in said production has been taught in Su et al; therefore, the reference is reasonably pertinent to the particular problem with which the applicants were concerned.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to PEGAH PARVINI whose telephone number is (571)272-2639. The examiner can normally be reached on Monday to Friday 8:00am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jerry Lorengo can be reached on 571-272-1233. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Pegah Parvini/
Examiner, Art Unit 1793

/Michael A Marcheschi/
Primary Examiner, Art Unit 1793